U.S. PATENT APPLICATION

FOR

IMPLANTABLE ARTERIOVENOUS SHUNT DEVICE

BY

JOHN L. FAUL, TOSHIHIKO NISHIMURA,

PETER N. KAO & RONALD G. PEARL

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is cross-referenced to and claims priority from U.S. Provisional Application 60/461,467 filed 04/08/2003, which is hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates generally to medical devices and methods. More particularly, the present invention relates to non-cardiac devices and methods that provide a fistula or lumen between the arterial system and venous system.

BACKGROUND

Chronic obstructive pulmonary disease affects millions of patients in the United States alone. The present standard of care is oxygen therapy, which requires a patient to remain near a stationary oxygen source or carry a bulky portable oxygen source when away from home or a treatment facility. It is easy to appreciate that such oxygen therapy has many disadvantages.

Lung reduction surgery has recently been proposed for treating patients with chronic obstructive pulmonary disease. Such surgery, however, is not a panacea. It can be used on only a small percentage of the total patient population, requires long recovery times, and does not always provide a clear patient benefit. Even when successful, patients often continue to require supplemental oxygen therapy.

For these reasons, it would be desirable to provide improved approaches, including both devices and methods, for treating patients suffering from chronic obstructive pulmonary disease. It would be desirable if such devices and methods were also useful for treating patients with other conditions, such as congestive heart failure, hypertension, hypotension, respiratory failure, pulmonary arterial hypertension, lung fibrosis, adult respiratory distress syndrome, and the like. Such devices and methods should provide for effective therapy, preferably eliminating the need for supplemental oxygen therapy in the treatment of chronic obstructive pulmonary disease. After the procedures, such devices and methods should optionally be adjustable so that the degree of therapy is responsive to the patient's needs at any particular time. At least some of these objectives will be met by the invention described hereinafter.

SUMMARY OF THE INVENTION

The present invention is a long-term implantable arteriovenous shunt device that can be used as a therapeutic method. The shunt device is implanted between an artery and a vein, preferably between the aorta and the inferior vena cava. The shunt device is implanted for a long-term period of at least 6 weeks and the implantation could be established via an open surgical procedure, a minimally invasive surgical procedure, or an intravascular procedure.

The objective of the shunt device is to decrease the systemic vascular resistance and allow a blood flow rate through the lumen of the shunt device of at least 5 ml/min after the implantation. The cross sectional area (or radius) and the length of the lumen of the shunt device are selected to having such a blood flow rate, with the cross sectional area in the range of about 19 mm^2 to about 750 mm^2, the length in the range of about 2.5 mm to about 15 mm, and the radius in the range of about 2.5 mm to about 15 mm. In one embodiment, the inner wall of the shunt device has a coating to prevent clot formation or atheroma formation.

In some situations it might be desirable to control the blood flow rate. Therefore, the present invention includes a control means to control the blood flow rate through the shunt at a desirable blood flow rate level or range. The control means could be as simple as an on/off mechanism (or switch), or could be more sophisticated by regulating the rate of flow ranging from either an open loop control or a closed loop control with feedback provided by physiological parameters. For each level of sophistication, the control means could include a controller (ranging from a switch to a decision algorithm), one or more flow control elements that control the rate of flow through the lumen, and/or one or more sensors to provide

feedback to a controller. Examples of physiological parameters that could be sensed or measure are blood pressure, heart rate, cardiac output, paO_2, O_2 saturation, O_2 saturation, mean systemic arterial pressure or mean systemic venous pressure.

In an alternate embodiment, the shunt device could a self-adjustable shunt device to self-adjust its cross sectional area or its length, or both, as a function of the pressure difference across the shunt device. The self-adjustable shunt could then automatically control the blood flow rate through the shunt at a predetermined blood flow rate level or range. The material of such a self-adjustable shunt device would then have expansion and contraction features to change the cross sectional area or the length, or both.

The reduction of systemic vascular resistance and (controlled) blood flow through the shunt device from the arterial system to the venous system has some important consequences that could benefit various kinds of patients. These consequences are related to respiratory, cardiac and circulatory effects. For example, the method could be a respiratory or cardio-respiratory therapy based on an increase of the partial pressure of O_2 dissolved in the arterial blood plasma, an increase of the hemoglobin O_2 saturation in arterial or venous blood, or an increase of the O_2 concentration in arterial or venous blood. Accordingly, patients with respiratory problems could benefit from the consequences as a respiratory or cardio-respiratory therapy. In another example, the method could be is a cardiac therapy based on an increase of the cardiac output. Accordingly, patients with cardiac problems could benefit from the consequences as a cardiac therapy. In yet another example, the method could be a circulatory therapy based on a decrease of the pulmonary arterial blood pressure, a decrease of the

systemic arterial blood pressure, a decrease of the systemic systolic pressure or a decrease of the systemic diastolic pressure. Accordingly, patients with circulatory problems could benefit from the consequences as a circulatory therapy.

BRIEF DESCRIPTION OF THE FIGURES

The objectives and advantages of the present invention will be understood by reading the following detailed description in conjunction with the drawings, in which:

FIG. 1 shows the concept of decreasing systemic vascular resistance according to the present invention;

FIG. 2 shows an example blood flowing, with or without a shunt device of the present invention, from a high resistance arterial system with a high oxygen concentration to the low resistance venous system with a low oxygen concentration;

FIG. 3 shows an example of shunt device positioned between the aorta and inferior vena cava according to the present invention;

FIG. 4 shows examples of shunt devices according to the present invention;

FIG. 5 shows an example of shunt device with a control means according to the present invention;

FIG. 6 shows an example of shunt device with a controllable or self-adjustable mechanism according to the present invention;

FIG. 7 shows an example of shunt device with a controllable mechanism based on a smart material according to the present invention;

FIG. 8 shows an example of a self-adjustable shunt device according to the present invention;

FIG. 9 shows an example of shunt device with a means to increase resistance to blood flow according to the present invention; and

FIGS. 10-12 show additional information regarding some physiological effects of an aorto-caval fistula in rats according to the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Blood flows from the heart via the arterial system **AS** to the vasculature of the tissues from which it returns back to the heart via the venous system **VS** as shown by system **110** in **FIG. 1**. Blood returning to the right side of the heart is pumped to the lungs where it binds oxygen (becomes oxygenated, or re-oxygenated) before returning to the left side of the heart to be pumped to the body's tissues via the arterial system. Blood flow experiences a resistance from all of the systemic vasculature, which is referred to as the systemic vascular resistance (SVR). SVR excludes the pulmonary vasculature but when these two are combined it is sometimes referred as total peripheral resistance (TPR). SVR is determined by factors that influence vascular resistance in individual vascular beds. Mechanisms that cause vasoconstriction (reducing the caliber of a vessel) will increase SVR, and those that cause vasodilation (increasing the caliber of a vessel) will decrease SVR. The actual change in SVR in response to neurohumoral activation, for example, will depend upon the degree of activation and vasoconstriction, the number of vascular beds involved, and the relative in-series and parallel arrangements of these vascular beds to each other. Although SVR is

primarily determined by changes in blood vessel diameters, changes in blood viscosity will also affect SVR.

The present invention decreases the SVR by having an arteriovenous shunt device **130** implanted to shunt and re-circulate blood from the arterial system **AS** to the venous system **VS** in system **120** as shown in **FIG. 1.** The re-circulated blood through shunt device **130** bypasses the peripheral microcirculation and decreases the SVR when one would compare system **110** with $\mathbf{SVR_0}$ to system **120** with $\mathbf{SVR_1}$; i.e. $\mathbf{SVR_1}$ is lower than $\mathbf{SVR_0}$. A desired decrease of the SVR would be at least 5% after the implantation of shunt device **130**.

In general, shunt device **110** could be implanted between a large (proximal) artery and a large (proximal) vein. The location is selected to shunt and (quickly) re-circulate blood from the high resistance arterial system with a high oxygen concentration to the low resistance venous system with a low oxygen concentration as shown by system **120** in **FIG 2**. In a preferred embodiment, implantation of shunt device **130** is between the aorta **310** and the inferior vena cava **320**, either proximal of the renal arteries, or more preferably distal of the renal arteries, as shown in **FIG. 3**.

Blood flow through a lumen **230** of the shunt device **130** typically results from a pressure gradient between the blood in the arterial system and the blood in the venous system, indicated by the large **P** and small **p** in **FIG. 2** (note different font sizes). The blood flow rate through shunt device **130** after implantation should be at least (about) 5 ml/min. While the pressure gradient between the arterial and venous sides of the vasculature will generally be

sufficient to achieve and control the target volume of blood flow, in some instances it may be desirable to utilize a control means or self-adjustable mechanism to either maintain a level/range or increase/decrease the blood flow rate (see also *infra*).

The reduction of SVR and (controlled) blood flowing through shunt device **130** from the arterial system to the venous system has some important consequences when system **110** (pre-implantation) and is compared with system **120** (post-implantation). These consequences are related to cardiac, circulatory and respiratory effects.

With respect to the cardiac effects, an important consequence of decreasing the SVR is that the cardiac output increases according to:

$$CO = \frac{MAP - CVP}{SVR}$$

whereby CO is cardiac output, MAP is mean arterial pressure, and CVP is central venous pressure. Since CVP is normally near 0 mmHg, the calculation is often simplified to:

$$CO = \frac{MAP}{SVR}$$

Cardiac output is equivalent to the blood flow rate according to:

$$CO = SV * HR$$

whereby SV is stroke volume and HR is heart rate.

When SVR decreases, MAP decreases to a smaller degree. The decrease in MAP is due to a small drop in systolic pressure ($P_{systolic}$) and a larger drop in diastolic pressure ($P_{diastolic}$). $P_{diastolic}$ is dependent on the SVR whereby a drop in SVR results in a drop in $P_{diastolic}$. The pulse pressure ($P_{systolic}$ - $P_{diastolic}$) is then increased. For instance, before implantation MAP could be 90 mmHg and SVR could be 18 dynes, which results in a CO of 5 liters per minute. SVR of 18 dynes is determined by dividing an SVR of 1440 dynes by a conversion factor of 80. MAP of 90 mmHg is determined by using:

$$MAP \cong P_{diastolic} + \frac{1}{3}(P_{systolic} - P_{diastolic})$$

with an exemplary PP of 30 mmHg given a $P_{systolic}$ of 110 mmHg and $P_{diastolic}$ of 80 mmHg.

After implantation, SVR could for instance drop from 1440 dynes to 1000 dynes and with the conversing factor of 80 drop from 18 to 12.5. If blood pressure has a $P_{systolic}$ of 100 mmHg over a $P_{diastolic}$ of 55 mmHg, then MAP is 70 mmHg; i.e. in this example the $P_{systolic}$ could have dropped by 10 mmHg, but the $P_{diastolic}$ could have dropped by 25 mmHg. Combining these exemplary numbers would result in a cardiac output of 5.6 liters per minute; i.e. 70 mmHg divided by 12.5.

With respect to the respiratory effects, an important consequence of shunting arterial blood to the venous circulation (such as the aorta to the inferior vena cava) is that blood with high O_2

content circulates to the venous blood system without having the O_2 extracted in tissue capillaries. The O_2 "rich" arterial blood re-circulates to, and mixes with, the low O_2 concentration of the venous system. As a result, the blood flowing through shunt device **130** increases the O_2 concentration in the venous blood, which is illustrated by the different (font) sizes of $\mathbf{O_2}$ in **FIG. 2**. The increase of O_2 concentration in the venous blood system leads to an increase in the O_2 concentration in the arterial blood in two ways, which is also illustrated by the different (font) sizes of $\mathbf{O_2}$ in **FIG. 2**. First, since the blood that is shunted does not have O_2 extracted by tissue capillaries, the blood returning to the lungs has a higher O_2 concentration after the creation of the shunt than before. Second, O_2 is carried in the blood in two forms: (i) dissolved in arterial plasma, and (ii) bound to a protein called hemoglobin that is contained in red blood cells. Oxygen binds to hemoglobin with curvilinear kinetics, so that O_2 very efficiently binds to (and is carried by) hemoglobin at high PaO_2 (partial pressure of O_2 in arterial plasma), but when the PaO2 is low (in particular below a PaO_2 of 60 mmHg), O_2 is less efficiently bound to (or carried by) hemoglobin. Since the amount of O_2 that is bound to hemoglobin is related to the PaO_2, an increase in PaO2 will result in greater binding of O_2 to hemoglobin, and increased oxygen carrying capacity.

With respect to circulatory effects, an important consequence of decreasing SVR is related to the fact that the lungs regulate their blood flow according to the O_2 content. A low O_2 content in the small pulmonary arteries impairs blood flow to the lung resulting in a high pulmonary pressure – a process called hypoxic pulmonary vasoconstriction. Therefore increasing the O_2 content in the pulmonary arterial blood should decrease the pulmonary arterial blood pressure. Other important circulatory consequences, as described *supra* with respect to cardiac

consequences, are a decrease in systemic arterial blood pressure, a decrease in systemic arterial systolic pressure and/or a decrease in systemic arterial diastolic pressure.

As a person of average skill in the art would readily appreciate, the different distinct effects could be beneficial to patients with cardiac problems as a cardiac therapy, to patients with respiratory problems as a respiratory or cardio-respiratory therapy, or to patients with circulatory problems as a circulatory therapy. An illustrative list of therapies is for instance:

- *Cardiac therapies*. The shunt device of the present invention could benefit patients with cardiac failure or patients who suffer from a low cardiac output (congestive heart failure) by providing an increased cardiac output.
- *Respiratory or cardio-respiratory therapies*. The shunt device of the present invention could benefit patients with pulmonary arterial hypertension to lower pulmonary arterial blood pressure, patients with heart and/or respiratory failure by increasing arterial oxygen concentration, patients with chronic obstructive pulmonary disease by increasing of blood oxygen concentration.
- *Circulatory therapies*: The shunt device of the present invention could benefit patients with hypertension to lower systemic arterial, systolic and/or diastolic blood pressure.

Other diseases or conditions that could benefit from the present invention are, for instance, hypotension (by increasing cardiac output), lung fibrosis, adult respiratory distress syndrome, and the like.

The blood flow rate through the shunt device is preferably at least 5 ml/min. In case the shunt device is a cylinder then the parameters of the lumen of the shunt device that determine the blood flow rate through its lumen can be determined with the Poiseuille equation:

$$BFR = \frac{\pi \Delta \Pr^4}{8\eta l}$$

whereby the volume flow rate (BFR) is a function of a blood with viscosity η, the pressure difference ΔP across the lumen of the shunt device, length ***l*** of the lumen of the shunt device and radius ***r*** of the lumen of the shunt device as shown by shunt device **410** in **FIG. 4**. One could also refer to the cross sectional area **CSA** of the lumen of shunt device **410**, which is in case of a cylinder equivalent to πr^2. Generally speaking, the shape of the lumen could be a circle, an oval or any other shape as long as the requirement of blood flow is met.

In an illustrative example using the Poiseuille equation, ΔP could range from about 30 mmHg (in someone with a MAP of 40mmHg and a venous pressure of 10 mmHg) to about 150 (in someone with a MAP of 160 mmHg and a venous pressure of 10 mmHg). The blood viscosity could be determined in a variety of ways that could for instance be obtained from a paper by Johnston BM et al. (2004) entitled "*Non-Newtonian blood flow in human right coronary arteries: steady state simulations*" and published in J Biomechanics 37:709-720. With a viscosity of 0.0345P and a combination of a radius of 3 mm and a length of 3 mm of the lumen of the shunt device one would achieve a blood flow rate through the shunt of over 5 ml/min. As a person of average skill would readily appreciate, different combinations of radius and length could be determined to achieve the desired blood flow rate. In general, the

length could range from about 2.5 mm to about 15 mm, and the radius could range from about 2.5 mm to about 15 mm. For the length one could determine a minimum length of e.g. 2.5 mm given an exemplary wall thickness of a human adult aorta of about 1.5 mm and an exemplary wall thickness of a human adult inferior vena cava of about 1 mm. One could also express the lumen opening in terms of cross section area, which could range from about 19 mm^2 to about 750 mm^2.

The shunt device is preferably made from any biocompatible material strong enough or sufficiently reinforced to maintain a lumen that meets the desired blood flow rate. In one embodiment, the shunt device is made of metal, preferably titanium, while in other embodiments the shunt device could be formed from conventional vascular graft materials, polytetrafluoroethylene (PTFE), nickel titanium memory, elastic material, or the like. The inner surface of the shunt device is preferably coated in whole or in part to inhibit the formation of blood clots. The surface could be coated with for instance polytetrafluoroethylene (Teflon®), or similar coatings/products. The shunt device might also be coated with antibiotic to prevent atheroma, infection, and/or anti-proliferative or anticoagulant agents to prevent clot formation in the lumen.

In a preferred embodiment, loosing the connection of the shunt device with the artery and vein should be avoided. Different techniques could be employed to provide such a secure connection. For instance, for attachment of shunt devices formed from typical fabric graft materials one could use sutures, staples, biocompatible glues, or the like. In the case of metals and other rigid materials, the shunt device could be formed with flared or flanged ends,

such as the umbrella or funnel device **424** (shown in **FIG. 4**). Umbrella ends **424** are placed at opposite ends of a tubular element **422** that form shunt device **420**. Umbrella ends **424** are positioned respectively inside the artery and inside the vein, and the tubular element connects in between the artery and the vein. In a different embodiment, umbrella ends **434** could be positioned more or less perpendicular with respect to tubular element **432** as shown in shunt device **430**. The key idea is that the diameter of the securing (connection) elements is larger than the opening in the artery and vein thereby keeping the shunt device in place. The securing elements could include a mechanism that unfolds when the shunt device is in place and implanted in the artery and vein. The art teaches different techniques and securing type mechanisms that could be used in the present invention.

The shunt device(s) could be implanted in a variety of ways, including the open surgical procedures, the laparoscopic and other minimally invasive techniques, and the intravascular techniques (where all or a portion of the shunt device is introduced at least partially through the lumen of one of the blood vessels to be shunted). The shunt device could also be implanted by, for instance, a surgical procedure such as an aortic surgery. The shunt device could further be implanted through interventional procedures such as, for instance, by means of a catheter through the iliac artery and guided by fluoroscopy. The shunt device could be deployed over a guidewire (e.g. the Seldinger technique) and assembled in the body through interventional radiology techniques like the opening of an umbrella. All such surgical and interventional techniques are well known in the art. It is preferred to leave the shunt device implanted in the person for a long-term period (at least 6 weeks, but most often for years).

In some cases it might be desired to include a control means to control the blood flow rate with one or more flow control elements, one or more controllers and/or one or more sensors. A flow control element **520** could be placed in the shunt device **510** as shown in **FIG. 5**. It could be placed at either end of the shunt device or somewhere in between. In one example, the function of the flow control element could be as simple as to have an electrically, magnetically or mechanically open/close mechanism such as a switch or one-way valve. Such an open/close element could also be a hook with a lever or a gearshift. In another example, a controller **530** could be used to control the timing of opening/closing (e.g. frequency and duration) or to control changes in blood flow rate. Controller **530** could control flow control element **510** such as one-way valve(s), pump(s) (positive displacement pump(s), rotary pump(s), peristaltic pump(s), and the like), controllable orifice(s) and the like. The flow control element could be electrically charged using an internal battery (e.g. a lithium battery; not shown) or by external power (not shown) using a magnetic impeller, both of which are common techniques in the art.

Yet another advancement of the control means for the shunt device is to include one or more sensors **540** that provide feedback to the controller **530**. The figures show two sensors, however, the present invention is not limited to two sensors and could be at least one sensor that is implanted inside the shunt device, near the shunt device, or inside or near the vasculature system. The sensor(s) could also be placed outside the body. Sensors **540** could sense (and/or measure) physiological parameter(s) in real time either periodically or continuously. The selection of one or more physiological parameters could be to reflect the condition of a person or patient who is being treated. Examples of physiological parameters

that could be sensed with one or more sensors are blood pressure, heart rate, cardiac output, paO_2, O_2 saturation, O_2 saturation, mean systemic arterial pressure, and/or mean systemic venous pressure. The controller could include a decision method to determine appropriate action on the flow control element. The controller could either be a stand-alone implantable controller and/or could be operated from outside the body. It might be useful to update the controller or change the current controller settings; e.g. in cases when the controller controls a set-value, a particular range or critical boundaries (minima/maxima), or when the controller requires an upgrade of its code.

The controller may select different criteria that are e.g. dependent on the type of disease, condition and/or desired therapy. In one example, the heart rate could be maintained at a reasonable physiological range and not exceed the person's maximum heart rate. The controller could have a target heart rate range of, for instance, 80 to 140 beats per minute, more usually from 90 to 110 beats per minute. In another example, it might be desired to increase cardiac output, partial pressure of O_2 dissolved in the arterial blood plasma (PaO_2), the hemoglobin O_2 saturation in arterial or venous blood, or the O_2 concentration in arterial or venous blood. These increases could be at least 5 % compared to their value before implantation, except for HbO_2, which could be at least 1%. In a preferred situation these increases could be higher and on the order of 10% or 20% and up (5% and 10% for HbO_2). In still another example, it might be desired to decrease the pulmonary arterial blood pressure, the systemic arterial blood pressure, the systemic systolic pressure or the systemic diastolic pressure. These decreases could be at least 5 % compared to their value before implantation. In a preferred situation these decreases could be higher and on the order of 10% or 20% and

up. In yet another example, the blood flow rate could increase from at least 5 ml/min compared to before implantation to a situation where the shunt is capable of carrying up to 5000 ml/min of blood at e.g. a pressure differential across the shunt device of 70 mmHg.

The description *supra* relates to a shunt device whereby the blood flow rate could be changed and controlled. In these situations, the structural parameters of the shunt device, such as the length, cross section area and radius are fixed. However, in an alternate embodiment, described *infra*, the shunt device could change its cross section area, radius and/or length. This could be accomplished either in a controlled fashion, like with a controller and sensor(s) as described *supra*, or in a self-adjustable fashion (i.e. self-organizing fashion).

FIG. 6 shows an example of a shunt device **610, 620** with a mechanism of leaves **630** disposed in the lumen of the shunt device that could change the cross section area of the lumen. Leaves **630** could be attached to a central axis or to the inner wall of shunt device **610, 620** respectively. Two or more leaves could be used with the capability of changing their position from a closed position gradually to an open position (compare **610** and **612**, and **620** and **622** respectively). The leaves in shunt devices **610, 620** could be integrated with a controller **640** and/or sensor(s) **650** in a similar fashion as described *supra*.

Leaves **630** could also be included as a self-adjusting mechanism for opening and closing of the shunt device. When the blood flow increases or blood pressure increases, the flexible

leaves automatically open up from a more or less closed position to a more or less open position, and *vice versa*.

FIG. 7 shows an example of a shunt device **710** that is made of a smart material such as a memory metal/alloy that can change its length and cross sectional area (radius). For instance, shunt device **710** could be made longer as shown by **720** or wider as shown by **730** (larger cross sectional area). Shunt devices **710** could be integrated with a controller **740** and/or sensor(s) **750** in a similar fashion as described *supra*. Mechanisms of memory metals/alloys (including particular stent-graft materials) and their controls are known in the art.

In a self-adjustable fashion it could e.g. be desirable to keep the blood flow rate at a level or range across the shunt device without any controller; i.e. the shunt device is self-organizing. To establish this the length and radius need to work in tandem as a function of ΔP and according to the Poiseuille equation (see *supra*) (see **FIG. 8**). For instance, length and ΔP have a linear relationship such that when ΔP increases the length increases in a linear fashion to maintain the blood flow rate at the same level, and *vice versa*. The radius and ΔP have an inverse non-linear relationship such that when ΔP increase the radius decreases in a non-linear fashion to maintain the blood flow rate at the same level, and *vice versa*. It is pointed out that the length and radius have to work in opposite and unequal value to maintain a particular blood flow rate (see *supra* for Poiseuille equation). Shunt device **810** should then be made of a material that is capable of increasing its length, but simultaneously decreasing its radius when ΔP increases, (indicated by changing from **810** and **820**). Examples of such

materials are elastic materials with reinforced filaments or fibers arranged and distributed over (or within) the shunt device (not shown in **810, 820**) to ensure selected and directional changes, according to Poiseuille equation; i.e. (i) an increase in cross sectional area with a decrease in length, and (ii) a decrease in cross sectional area with an increase in length.

Other than following the Poiseuille equation one could change the blood flow rate by following Ohm's law by increasing the resistance to blood flow through the shunt device. Means to increase this resistance could for instance be accomplished by disposing roughness or obstacles such as bumps **930** or filaments/spokes **940** to the inner wall of the lumen of shunt device **910, 920** respectively as shown in **FIG. 9**. The blood flow could then also change from laminar flow to non-laminar flow.

FIGS. 10-12 show additional information regarding some physiological effects of an aorto-caval fistula in rats. These effects are the result of a study performed by the inventors of the present invention. **FIG. 10** shows the effect of an aorto-caval fistula on several groups of experimental animals. In each group the presence of an aorto-caval fistula was associated with increased aortic blood flow (AF) and with increased partial pressure of oxygen in arterial blood (PaO_2) in rats that were receiving supplemental oxygen ($FiO_2 = 0.24$, or the fraction of inspired oxygen was 24%). Measurements of: (A): Aortic flow (24% O2) and (B): Arterial blood oxygen tension (FiO_2=0.24) (PaO_2). Note that groups PM and PFM received FiO_2=0.50 during experimentation. Group N represents normal rats (n = 6), Group F underwent aorto-caval fistula (n = 6), Group P underwent left pneumonectomy (n = 6), Group

PF underwent left pneumonectomy and the creation of an aorto-caval fistula ($n = 6$), Group M received a toxin that causes pulmonary hypertension called monocrotaline ($n = 6$), Group FM underwent aorto-caval fistula and received monocrotaline ($n = 6$), Group PM underwent left pneumonectomy and received monocrotaline ($n = 6$), Group PFM underwent left pneumonectomy and the creation of an aorto-caval fistula and then received monocrotaline ($n = 6$). (** = $p < 0.01$).

FIG. 11 shows the effect of the presence of an aorto-caval fistula in several groups of experimental animals. Aorta-caval fistuala attenuates the development of pulmonary arterial hypertension. The measurements shown in **FIG. 11** are of mean pulmonary artery pressures (PAP). Group N represents normal rats ($n = 6$), Group F underwent aorto-caval fistula ($n = 6$), Group P underwent left pneumonectomy ($n = 6$), Group PF underwent left pneumonectomy and the creation of an aorto-caval fistula ($n = 6$), Group M received monocrotaline ($n = 6$), Group FM underwent aorto-caval fistula and received monocrotaline ($n = 6$), Group PM underwent left pneumonectomy and received monocrotaline ($n = 6$), Group PFM underwent left pneumonectomy and the creation of an aorto-caval fistula and then received monocrotaline ($n = 6$). (* = $p < 0.05$, ** = $p < 0.01$).

FIG. 12 shows photomicrographs of small pulmonary arteries (A–D). (A) shows an example that normal rat (group *N*) arterioles do not have evidence of neointimal formation (*grade 0*). (B) shows an example of a *grade 1* neointimal lesion (< 50% occlusion) seen in rats that received monocrotaline alone (group M). (C) shows an example of *grade 1* neointimal lesion

(< 50% occlusion) seen in rats that underwent left pneumonectomy and the creation of an aortocaval fistula (ACF) and then received monocrotaline (group PMF). (D) shows an example of a *grade 2* neointimal lesion (> 50% occlusion) seen in rats that underwent left pneumonectomy and received monocrotaline (group PM). All photomicrographs (X400), elastin van Gieson stain.

The present invention has now been described in accordance with several exemplary embodiments, which are intended to be illustrative in all aspects, rather than restrictive. Thus, the present invention is capable of many variations in detailed implementation, which may be derived from the description contained herein by a person of ordinary skill in the art. For example, in some instances, it may be possible and desirable to implant two or more shunt devices at different locations between the arterial and venous sides of the vasculature. In cases of such multiple shunt device implantations, the individual shunts may be implanted in close proximity to each other or may be distributed at different regions of the vasculature.

In another aspect, it should be pointed out that the present invention could be used as preventative care or as a therapy for a condition or disease. Furthermore, as a person of average skill would readily appreciate, the long-term implantable shunt device could be beneficial to improve the performance in athletes, military service personnel, performance animals (e.g. dogs and horses).

The preferred location of the shunt device is between the aorta and inferior vena cava as described *supra*. However, it would be feasible to implant one or more shunt devices for a long-term period in the pelvis area to link the common iliac artery and vein or femoral artery and vein. In another embodiment the shunt device could be positioned in the axilla and it would link the axillary artery and vein. In yet another embodiment the device could be positioned close to the clavicle and link the subclavian artery and vein.

All such variations and other variations are considered to be within the scope and spirit of the present invention as defined by the following claims and their legal equivalents.